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The Potential of Noni (*Morinda citrifolia L.*) as an Antidiabetic

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Abstract

Background: Diabetes Mellitus (DM) is a growing global health issue, with Type 2 diabetes accounting for 90% of cases. Insulin resistance leads to hyperglycemia. Management involves a healthy lifestyle and pharmacological therapy. However, side effects can be managed with alternative therapies like noni, an herbal ingredient being studied for potential antidiabetic properties.

Objective: The study aims to review and learn more about the potential of noni (*Morinda citrifolia L.*) as an antidiabetic.

Methods: This research is literature review. The kinds of literature are English and Indonesian language research articles related to the topic searched by using database sources from ProQuest, PubMed, ScienceDirect, and Google Scholar. The research articles were published in the last ten years (2012 to 2022).

Results: 14 kinds of literature match the topic of study. A total of 12 kinds of literature are in vivo studies on animals and two literature studies on humans. The result shows that noni has an antidiabetic effect by lowering blood glucose levels and improving other parameters. Parts of Noni that have the potential to control Type 2 DM are fruit and leaves, which can be in the form of extracts, juices, or fermented products. Further research is needed to evaluate the toxicity, the content of active compounds, and the expression of genes related to Type 2 DM to ensure the mechanism of noni in controlling hyperglycemia. Human studies with more respondents are also needed to confirm the findings of existing studies.

Conclusion: Noni has an antidiabetic effect by lowering blood glucose levels and improving other parameters. Based on human studies, noni fruit juice can serve as a suitable addition to the diet of Type 2 DM patients.

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INTRODUCTION

Diabetes Mellitus (DM) is still a significant health problem in the world today because the prevalence remains increasing. Based on data from the IDF (International Diabetes Federation), as many as 537 million people in the world have diabetes in 2021. This number is expected to increase to 643 million people in 2030 and 783 million people in 2045[1]. Type 2 diabetes mellitus is the most common type of diabetes mellitus, which accounts for about 90% of all diabetes cases. In general, this disease is characterized by insulin resistance, a condition in which the body does not fully respond to the presence of insulin. As a result, glucose levels in the blood continue to increase (hyperglycemia). Type 2 DM is most common in adults but is being diagnosed more and more in children, adolescents, and young adults. This reality is related to the increasing incidence of obesity, lack of physical activity, and poor diet[2].

Several risk factors associated with type 2 DM include a family history of diabetes, overweight, unhealthy diet, lack of physical activity, age, high blood pressure, race, impaired glucose tolerance, history of gestational diabetes, and poor nutrition during pregnancy. Type 2 DM is associated with complications, such as atherosclerosis, which can cause stroke, ischemic heart disease, kidney failure, and retinopathy, which can result in blindness[2].

The most important management of Type 2 DM is a healthy lifestyle, such as a healthy diet, regular exercise, not smoking, and maintaining body weight to stay within normal limits[1]. In addition, pharmacological therapy is also needed to keep blood glucose levels in people with diabetes under control. However, antidiabetic drugs can cause some side effects, such as metabolic and gastrointestinal disturbances, hypoglycemia, increasing risk of cardiovascular disease, etc.[3]. Therefore, the development of alternative diabetes therapy is needed to minimize side effects.

One of the herbal ingredients being studied for its potential as an antidiabetic is noni (*Morinda citrifolia L.*). Noni fruit and leaves have been used as food and medicine by the indigenous people of Southeast Asia and the Polynesian Triangle for hundreds of years. Noni is one of the most important medicinal plants for Polynesian people, one of which is anti-diabetic[4]. The study aims to review and learn more about the potential of noni as an antidiabetic.

METHODS

This research is included in the literature review. Articles were searched using ProQuest, PubMed, ScienceDirect, and Google Scholar database sources. The literature review included Indonesian and English research articles on the potential of noni as an antidiabetic, either in fruit, leaves, or other parts of the noni plant. The search is limited to research articles published within the last ten years, namely 2012 to 2022, which can be accessed in full text in PDF format. This study did not use types of review articles (systematic or literature reviews). A literature search was carried out using the keywords "(Morinda citrifolia L. or noni or noni) AND (diabetes)." Obtained literature, then analyzed, compared, discussed, and concluded.

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RESULTS

Fourteen kinds of literature match the topic of study. A total of 12 kinds of literature are in vivo studies on animals and two literature studies on humans.

Table 1 Study of the potential of noni as an antidiabetic in experimental animals

No	Title/ Author /Year	Objective	Sample Size and Methods	Results
1.	The Effect of Noni Leaves Extract on Blood Glucose Levels in Streptozotocin-Induced White Rats/ Wulandari *et al.*/ 2022	To evaluate the effect of noni leaves extract on blood glucose levels in streptozotocin-induced white rats.	30 male white rats (6 groups) I: negative control (CMC Na) II: positive control (glibenclamide 0.45 mg/kg BW) III: Noni ethanol leaves extract in 250 mg/kg BW dose IV: Noni ethanol leaves extract in 500 mg/kg BW dose V: noni ethanol leaves extract in 750 mg/kg BW dose Blood glucose levels were measured on days 0, 7, 14, 21, and 28	The ethanol extract of noni leaves contains secondary metabolites, such as alkaloids, flavonoids, tannins, saponins, and steroids. Administration of noni ethanol leaf extract in doses of 250, 500, and 750 mg/g BW reduced blood glucose levels but did not have an effective dose in reducing blood glucose levels in streptozotocin-induced male white rats.
2.	Antihyperglycemic Effects of Noni Fruit (*Morinda citrifolia L.*) Fractions on Male White Rats/ Mukhriani *et al.*/ 2018	To evaluate the effects of noni fruit fractions on male white rats.	15 male white rats (5 groups) I: negative control (CMC 1%) II: positive control (glibenclamide 0.09 mg) III: Fraction A (ethylacetate: methanol= 20:1, 15:1, and 10:1) IV: Fraction B (ethyl acetate: methanol = 5:1 and 1:1; chloroform: methanol = 20:1, 15:1, dan 10:1) V: Fraction C (chloroform: methanol = 5:1 and 1:1) Dose of fraction = 1000 mg/kg BB Blood glucose levels were measured 0, 30, 60, and 90 minutes after intervention.	The average decrease in blood glucose levels (mg/dL) I = 39 II = 141 III = 131 IV = 113 V = 79 Fraction A had the highest antihyperglycemic effect with a blood glucose reduction rate of 55.77%, like glibencla-mide as a positive control with a blood glucose reduction rate of 60.06%.
3	Effect of Noni Fruit Juice (*Morinda Citrifolia L.*) on Blood Glucose Levels in	To evaluate the effect of noni fruit juice on blood glucose levels in	25 Wistar strain male white rats (5 groups) I: negative control (CMC Na 1%) II: positive control (glibenclamide 1.89 mg/kg BW) III: Dose I (noni fruit juice 1.22 mg/kg BW)	There was a significant difference ($p < 0.05$) between the negative control, positive control, and all three doses of noni intervention).

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No	Title/ Author /Year	Objective	Sample Size and Methods	Results
	Wistar Strain Male White Rats Burdened by Glucose / Lidia/ 2016	Wistar strain male white rats burdened by glucose.	IV: Dose II (noni fruit juice 2.44 mg/kg BW) V: Dose III (noni fruit juice 4.89 mg/kg BW) Administration of glucose = 2 g/kg BW. Blood glucose levels were measured at 0, 30, 60, 120, 180, 240, and 300 minutes after glucose administration.	Hypoglycemic power (%) II= 36.50 III= 32.50 IV= 31.68 V= 27.47
4.	Test Several Doses of Noni Fruit Extract (*Morinda citrifolia* L.) on Blood Glucose Levels in Alloxan-Induced Wistar (*Rattus norvegicus*) Rats / Zega *et al.*, / 2016	To find out the minimum dose of noni fruit extract on blood glucose levels in alloxan-induced Wistar rats	25 Wistar rats (5 groups) I: negative control (Aquades) II: positive control (Insulin Novomix 0.4 IU/100 g BW) III: Noni fruit extract 125 mg/kg BW IV: Noni fruit extract 250 mg/kg BW V: Noni fruit extract 500 mg/kg BW Blood glucose levels were measured seven times on day 1 (H1) and day 2 (H2): 0, 6, 12, 18, and 24 hours after the intervention.	All three doses have a glucose-lowering effect in the first 6 hours after the intervention. Noni fruit extract at 125 mg/kg BW already affects lowering blood glucose levels.
5.	Effect of Noni Fruit Juice (*Morinda citrifolia Linn.*) to Glibenclamide on Reducing Blood Glucose Levels in Diabetes Male White Rats/ Sari *et al.* / 2012	To evaluate the effect of noni fruit juice to glibenclamide on reducing blood glucose levels in diabetes male white rats	24 Sprague Dawley male white rats (6 groups) KN: Normal Control (CMC 0.5% atau 1 mL/200 g BB) KD: Diabetes Control (diabetes, given by CMC 0.5% or 1 mL/200 g BW) KG: Glibenclamide Control (Glibenclamide 0.9 mg/200 g BW) KM: Noni Control (noni fruit juice 2.5 mL/200 g BW) ID1: Dose 1 interaction (diabetes, given by Glibenclamide 0.9 mg/ 200 g BW and noni fruit juice 2.5 mL/200 g BW) ID2: Dose 2 interaction (diabetes, given by Glibenclamide 0.9 mg/ 200 g BW and noni fruit juice 5.0 mL/200 g BW) Blood glucose levels were measured on the day alloxan- induced days of intervention (days 1, 8, 15, and 22)	Administration of noni fruit juice significantly affected glibenclamide in reducing blood glucose levels in diabetic male white rats in the combination of glibenclamide 0.9 mg/200 g BW and noni juice 5.0 mL/200 g BW after two weeks of administration.
6.	Hypoglycemic Effects of *Morinda citrifolia*	To evaluate the effects of noni fruit	30 Wistar male white rats (5 groups) I: without intervention	Group V showed the most significant decrease in blood glucose among the other treatment groups.

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No	Title/ Author /Year	Objective	Sample Size and Methods	Results
	Fruit Juice in Diabetic Rats/ Achmad and Jenie / 2012	juice on diabetic control.	II: alloxan induction III: Noni fruit juice 2.25 g/kg BW IV: Noni fruit juice 4.5 g/kg BW V: jus buah mengkudu 9 g/kg BW Noni fruit juice was given for seven days. Blood glucose levels were measured on days 8, 11, 18, and 26	There was a significant difference between the control and treatment groups. Administration of noni fruit juice doses of 2.25 g/kg BW, 4.5 g/kg BW, and 9 g/kg BW for seven days can reduce blood glucose levels in male diabetic Wistar rats.
7	Antidiabetic Test of Water, Ethyl Acetate, and n-hexane Fraction of Noni Fruit (*Morinda citrifolia L.*) in Alloxan-Induced White Rats / Musfiroh *et al.*/ 2020	To evaluate the antidiabetic activity of the water, ethyl acetate, and n-hexane fractions of noni fruit in alloxan-induced white rats and to determine the best blood glucose lowering activity fractions.	28 male white rats (6 groups) KN: PGA 2% (not alloxan-induced) KN (-) : PGA 2% + alloxan-induced KN (+) : PGA 2% + glibenclamide + alloxan-induced Test I: 1.2 g/kg BW water fraction in PGA 2% + alloxan-induced Test II: 1.2 g/kg BW ethyl acetate fraction in PGA 2% + alloxan-induced Uji III:1.2 g/kg BB n-hexane fraction in PGA 2% + alloxan-induced	Administration of the water, ethyl acetate, and n-hexane fraction of the ethanol extract of noni fruit showed significant blood glucose lowering activity when compared to the negative control. On the fifth day, the treatment of the n-hexane fraction of the noni fruit ethanol extract provided the best decrease in blood glucose levels (71.99%) compared to the decrease in blood glucose levels of the water and ethyl acetate fractions.
8	Hypoglycemic Activity and Pancreas Protection of Combination of *Morinda citrifolia Linn.* Juice and *Curcuma xanthorrhiza Roxb.* Juice on Streptozotocin- Induced Diabetic Rats/ Santoso *et al.* /2018	To evaluate the hypoglycemic activity and pancreas protection of a combination of *Morinda citrifolia Linn.* and *Curcuma xanthorrhiza Roxb.* juice on streptozotocin-induced diabetic rats	35 rats (7 groups) I: normal group II: negative control III: positive control (Glibenclamide 4.5mg/kg BW) IV: Combination 1 (*mengkudu fruit juice*/ MFJ: *temulawak rhizome juice*/ TRJ = 1/8:1/8) V: Combination MFJ: TRJ = ¼: ¼ VI: Combination MFJ: TRJ = ½: ½ VI: Combination MFJ: TRJ = 1: 1 All groups (except the normal group) were treated for 28 days.	Diabetic rats were given the combination of MFJ-TRJ and have a significant value in decreasing blood glucose and MDA levels and improvements in pancreatic morphology compared to the negative control group. The combination of MFJ-TRJ (1:1) has hypoglycemic activity, and MFJ- TRJ (⅛:⅛) can improve pancreatic morphology

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			Blood glucose levels were measured on days 8, 15, 22, and 29. On day 29, an analysis of MDA (malondialdehyde) levels was carried out. At the end of the treatment, termination was carried out to analyze the morphological conditions of the pancreas.	
9	Effect of Mixture of Mengkudu and Temulawak Juices on MDA Levels and SOD Activity in Streptozotocin-induced Diabetic Rats Liver / Santoso *et al.*/ 2015	To evaluate the effect of a mixture of mengkudu and temulawak juices on MDA levels and SOD activity in streptozotocin-induced diabetic rats' liver	21 rats (7 groups) N: Normal NC: negative control (diabetic rats) PC: positive control (Glibenclamide 4.5mg/kg BW) Intervention group MT (mengkudu fruit juice/ MFJ: temulawak rhizome juice/ TRJ = ml/kg BW/day) MT1 : (MFJ : TRJ = 3.6 : 10) MT2 : (MFJ : TRJ = 1.8 : 5) MT3 : (MFJ : TRJ = 0.9 : 2.5) MT4 : (MFJ : TRJ = 0.45 : 1.25) The treatment was carried out for 28 days.	The average of MDA levels (nmol/g) N = 2.79; NC = 7.86; PC = 4.25; MT1 = 4.14; MT2 = 4.91; MT3 = 5.68; MT4 = 5.72 The average of SOD levels (nmol/g) N = 75.00; NC = 13.69; PC = 53.57; MT1 = 56.55; MT2 = 46.43; MT3 = 30.95; MT4 = 33.93 A mixture of noni and temulawak juice can reduce liver MDA levels by up to 47.33% and increase liver SOD activity by up to 313.07% when compared to negative control.
10	Effect of Addition of Noni (*Morinda citrifolia L.*) Juice to White Bread on Blood Glucose Levels in Alloxan-Induced Rats/ Laelatunisa *et al.*/ 2019	To evaluate the effect of the addition of noni fruit juice to white bread on blood glucose levels in alloxan-induced rats	21 white mice (7 groups) I: negative control II: positive control III: intervention 1 (white bread without noni fruit juice) IV: intervention 2 (white bread + noni fruit juice 50 mL) V: intervention 3 (white bread + noni fruit juice 150 mL) VI: intervention 4 (white bread + noni fruit juice 250 mL) VII: intervention 5 (noni fruit juice 0.2 mL) Blood glucose levels were measured at 30 and 60 minutes after the intervention	The addition of 250 mL of noni fruit juice on white bread gives blood glucose lowering activity up to 37.65% after 60 minutes of consumption. Alkaloids were detected in white bread added with noni juice.
11	Modulatory effect of Mengkudu fruit on the activities of key en-	To screen the secondary metabolites and evaluate the	24 rats (4 groups) 1: Control rats 2: diabetic rats induced by STZ	Administration of MFE orally to diabetic rats: Increase the activity of hexokinase, pyruvate kinase, LDH, and glucose-6-phosphate-dehydrogenase

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No	Title/ Author /Year	Objective	Sample Size and Methods	Results
	zymes of glucose synthesis and utilization pathways of diabetic induced rats/ Haque dan Rao/ 2013 (Haque dan Rao, 2013)	ameliorative potential of ethanolic extract of Morinda citrifolia (Mengkudu) Fruit Extract (MFE) on the glucose synthesis and utilization reactions.	3: diabetic rats with MFE intervention (300 mg/kg BW/rat/ day) 4: diabetic rats with gliclazide intervention (5 mg/kg BW/rat/ day) The intervention for groups 3 and 4 rats was given in the form of a liquid suspension orally for 30 days	Reduce the activity of glucose-6-phosphatase fructose-1,6-bisphosphatase in liver and kidney tissue; reduce glycogen phosphorylase in liver tissue.
12	Antidiabetic Effect of *Morinda citrifolia* (Noni) Fermented by *Cheonggukjang* in KK-A^{y} Diabetic Mice/ Lee *et al.*/ 2012	To evaluate the antidiabetic effect of *Morinda citrifolia* (noni) fermented by *Cheonggukjang* in KK-A^{y} diabetic mice	28 KK-Ay male rats/ Type 2 DM TaJcl and obesity (4 groups) DC: diabetic control PC: positive control (given Banaba leaves or *Lagerstroemia speciosa*, foods to regulate blood glucose levels) MC: given *dried M. citrifolia fruit powder* FMC: given *Fermented M. citrifolia*	Blood glucose levels in the FMC group during the 90-day intervention period were 211.60–252.20 mg/dL, whereas in the control group, they were 400 mg/dL after 20 days of intervention. Administration of FMC also reduced HbA1c levels, increased insulin sensitivity, and significantly reduced serum triglyceride and LDL levels. Fermented M. citrifolia 70% ethanolic extract (FMCE) activates peroxisome proliferator-activated receptor-γ (PPAR-γ) and stimulates glucose uptake through activation of AMP-protein kinase (AMPK) in C2C12 cell culture.

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Table 2 Study of the potential of noni as an antidiabetic in human

No	Title/ Author /Year	Objective	Sample Size and Methods	Results
1.	The Effect of *Morinda citrifolia L.* Fruit Juice on the Blood Sugar Level and Other Serum Parameters in Patients with Diabetes Type 2/ Algenstaedt *et al.* / 2018	To evaluate the effect of *Morinda citrifolia L.* fruit juice on the blood sugar level and other serum parameters in patients with diabetes type 2	20 patients with diabetes type 2 The juice consists of 89% fermented noni fruit puree harvested from French Polynesia, mixed with 11% blueberry juice and red wine to mask the unpleasant taste of the Noni fruit. Patients consumed 2 mL/kg of noni juice daily for eight weeks. Blood samples were taken before consumption and 4 and 8 weeks after consumption. Fasting blood glucose levels were measured every 1 or 2 days during the juice consumption.	Blood glucose levels (mg/ dL) Pre-intervention= 139±23 Post-intervention= 125±22 *p-value* =0.0024 (significant) Reduction of HbA1c levels (mg/dL) = 0.27±0.5%, d p=0.033 (significant) Elevation of C-peptide levels (µg/L) After 4 weeks = 0.35 ± 1.26 (p=0.25, not significant) After 8 weeks = 0.33 ± 1.99 (p=0.49, not significant) Total cholesterol (mg/ dL) Pre-intervention = 258 ± 50 Post-intervention = 248 ± 43 p= 0.07 (not significant) HDL levels (mg/ dL) Pre-intervention = 41.0 ± 10.6 After 4 weeks = 42.3 ± 10.3 After 8 weeks = 41.75 (not significant) Reduction of hs-CRP levels p=0.01 (significant)
2.	The Potential of Noni (*Moringa citrifolia*) in Lowering Blood Glucose Levels in Diabetes Mellitus Patients/ Dafriani *et al.*/ 2020	To evaluate the potential of noni in lowering blood glucose levels in diabetes mellitus patients	16 type 2 DM patients Control group = 8 patients Intervention group = 8 patients	Blood glucose levels (mg/ dL): Control group = 326.25 Intervention group = 199.88 P= 0.003 (significant)

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DISCUSSION

Morinda citrifolia L. is a plant that belongs to the Rubiaceae family. This plant is known as noni, or in Indonesia, it is called 'mengkudu.' The indigenous people of Polynesia have used the noni plant to treat diabetes for hundreds of years. After 1996, noni fruit juice became very popular as a health drink worldwide. Noni has been reported to have many health benefits for treating cancer, infections, arthritis, diabetes, asthma, hypertension, and pain. All parts of this plant, such as roots, stems, bark, leaves, flowers, and fruit, have been recorded to be used as a combination of nearly 40 well-known herbal medicines. The main components of the noni plant include scopoletin, octanoic acid, potassium, vitamin C, terpenoids, alkaloids, anthraquinones, β-sitosterol, carotene, vitamin A, linoleic acid, and amino acids5.

Study of the potential of noni as an antidiabetic in experimental animals

Based on the literature, studies in experimental animals show that noni has potential as an antidiabetic by reducing glucose levels in the intervention group and improving several other parameters. This effect can be learned from 12 research articles that measure glucose levels and other parameters on the effects of noni administration in experimental animals. Doses of 250, 500, and 750 mg/g BW noni leaves ethanol extract reduced blood glucose levels in streptozotocin-induced male white rats but did not have the most effective dose[6]. This condition is due to the unknown number of secondary metabolites in the noni leaf's ethanol extract, which can reduce blood glucose levels to normal levels. This study also conducted phytochemical tests. The results showed that the ethanol extract of noni leaves contained alkaloids, flavonoids, saponins, tan-nins, and steroids. Alkaloids can neutralize toxins in the body and regenerate β-pancreatic cells damage because they have detoxifying properties[7]. Flavonoids can inhibit the formation of free radicals and can regenerate pancreatic β-cells due to their role as antioxidants, thereby increasing insulin secretion. Saponins can reduce the absorption of food extracts and lower blood glucose levels by inhibiting glucose transport in the digestive tract and stimulating insulin secretion[8].

Noni fruit in extract form at a dose of 125 mg/kg BW reduced blood glucose levels in alloxan-induced Wistar rats (*Rattus norvegicus*)[9]. The decrease in glucose levels is probably caused by the natural precursor in noni fruit, namely proxeronin. Proxeronin is converted into xeronin alkaloids in the body by the proxeroninase enzyme[10]. Xeronin is a relatively small alkaloid, which is physiologically very active and plays an essential role in the function of all body cells. At the molecular level, Xeronin works to repair damaged cells. In this study, xeronine is thought to play a role in repairing damaged pancreatic β-cells so that insulin secretion works properly and can reduce blood glucose levels [9].

Noni fruit extract into three fractions was also evaluated to determine the antihyperglycemic effect in white male rats. The results showed that Fraction A, with the eluent ratio of Ethyl Acetate: Methanol was 20:1, 15:1, and 10:1, had a more significant antihyperglycemic effect than Fractions B and C, with an average decrease in blood glucose of 130.67 mg/day dL or 55.77% within 90 minutes. The decrease in blood glucose was like that of glibenclamide as a positive control rat, which was 60.06%. This condition is suspected to have occurred because the content of active compounds in fraction A was higher than that of fractions B and

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C. The results of the identification test for the compound showed the presence of triter-penoids, flavonoids, organic compounds, and phenolics in fraction A[11]. Ethanol extract of noni fruit was used to determine its antidiabetic activity in the water, ethyl acetate, and n-hexane fractions in alloxan-induced white rats. The results showed that treatment of the n-hexane fraction of noni fruit ethanol extract on day 5 provided the best reduction in blood glucose levels compared to the water and ethyl acetate fractions of the negative control, which was 71.99%. Therefore, the n-hexane fraction had the best blood glucose-lowering activity compared to the other groups[12].

Noni fruit in extract form is also used to evaluate its potential as antidiabetic. Ethanol extract of Noni fruit (MFE) administration was used to determine its role in glucose utilization and synthesis reactions and its secondary metabolite content. The results showed that MFE administration orally to diabetic rats increased the activity of hexokinase, pyruvate kinase, LDH, and glucose-6-phosphate-dehydrogenase. These enzymes increase the effectiveness of glucose utilization. Increasing glycogen synthase activity illustrates the high glycogen in the liver. In addition, the decreasing activity of glucose-6-phosphatase, fructose-1,6-bisphosphatase in liver and kidney tissues, and glycogen phosphorylase in liver tissue after administration of MFE showed a decrease in endogenous glucose production through gluconeogenesis and glycogenolysis. MFE can improve glycemic status by regulating key enzymes that play a role in carbohydrate metabolism in the hepatic and kidney tissues of diabetic rats. Further research is needed to determine the expression of these critical enzymes to ensure the mechanism of MFE in controlling hyperglycemia[13].

Several in vivo studies on experimental animals used noni fruit juice to evaluate its effect as an antidiabetic [14,15,16,18,19,20,26,27,29]. There was a significant difference between the negative control, positive control, and all three doses (1.22 mg/kg BW, 2.44 mg/kg BW, and 4.89 mg/kg BW) of noni fruit juice intervention in male white Wistar rats burdened with glucose 2 g/kg BW. This study shows that noni fruit juice has a hypoglycemic effect in all dose groups. This hypoglycemic effect may be caused by active compounds that play a role in the mechanisms, such as increasing insulin secretion, reducing serum glucagon levels, acting like insulin, and increasing the potential for insulin action. However, it is not known exactly what type of active compound and the mechanism that causes the hypoglycemic effect of noni fruit juice[14]. Administration of noni fruit juice also had a significant effect on glibenclamide in lowering blood glucose levels in the combination of 0.9 mg/200 g BW of glibenclamide and 5.0 mL/200 g of noni juice after two weeks of treatment in diabetic male white rats of the Sprague Dawley strain. This result indicates a synergistic interaction between glibenclamide and noni juice in lowering blood glucose levels. Both are suspected to have a similar mechanism of action, that is, triggering pancreatic β-cells to secrete insulin, thereby lowering glucose levels in the blood[15].

Noni fruit juice was also used to evaluate its effect on blood glucose levels in male white rats of the Wistar strain. The results showed that all intervention doses affected lowering blood glucose levels, but a dose of 9 g/kg BW group showed the most significant decrease in

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blood glucose among the other intervention groups. Based on the statistical analysis results, there was also a significant difference between the control and intervention group[16]. The hypoglycemic effect is thought to be due to noni fruit containing saponins and flavo-noids[17]. Both compounds can trigger insulin secretion.

A combination of noni and temulawak juice was used to determine its effect on hypoglycemic activity and pancreatic protection in Streptozotocin-induced diabetic rats. The results showed that the combination of MFJ (mengkudu fruit juice) – TRJ (temulawak rhizome juice) with a ratio of 1:1 had hypoglycemic activity, and MFJ-TRJ (⅛:⅛) could improve pancreatic morphology[18]. This study previously used the same research materials and experimental animals in 2015. However, the parameters studied were levels of MDA (Malondialdehyde) and SOD (superoxide dismutase) activity[19]. A mixture of noni juice and ginger can reduce liver MDA levels by up to 47.33% and increase liver SOD activity by up to 313.07% when compared to negative controls. The decrease in blood glucose and MDA levels by giving a mixture of noni and ginger juice is thought to be caused by the content of scopoletin and curcumin compounds or other compounds that can act as antioxidants. Scopoletin is a derivative of coumarin, which can protect against hyperglycemia and insulin resistance [20]. Curcumin has antioxidant activity and can prevent free radicals[21]. Curcumin can enhance the immune system [22,23] and antidiabetic [24]. MDA is a lipid peroxidation product whose levels can be reduced by the presence of antioxidant compounds as electron donors to free radicals. Low levels of MDA indicate inhibition of lipid oxidation by antioxidants. While increasing SOD activity can reduce oxidative damage to rat livers[25].

Adding noni fruit juice to white bread was evaluated to determine its effect on blood glucose levels in alloxan-induced rats. Adding 250 mL of noni extract to plain bread provided a blood glucose-lowering activity of up to 37.65% after 60 minutes of consumption. In this study, identification of secondary metabo-lites was also carried out. White bread added with noni extract was detected to contain alkaloid compounds, as indicated by the intensity of the orange color getting stronger when more noni juice was added through the Dragendorf test[26]. The decrease in blood glucose levels is thought to be caused by the presence of xeronine compounds[27]. Xeronine belongs to the alkaloid class that results from conversion from the natural precursor in noni, namely proxeronine. Xeronine is believed to help reduce high blood pressure and blood glucose[5].

Noni fruit fermented by Cheonggukjang was used to determine its antidiabetic effect in KK-Ay diabetes rats. The results show that the administration of FMC can lower blood gluco-se levels. FMC administration also reduced HbA1c levels, increased insulin sensitivity, and lowered serum triglyceride and LDL levels. Fermented M. citrifolia 70% ethanolic extract (FMCE) activates peroxisome proliferator-activated receptor-γ (PPAR-γ) and stimulates glucose uptake through activation of AMP-protein kinase (AMPK) in C2C12 cell culture. PPAR-γ can improve insulin sensitivity and glucose tolerance by regulating lipid storage, glucose homeostasis, and adipokine production. Therefore, FMC can be a functional health food for managing Type 2 DM[29].

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Study of the potential of noni as an antidiabetic in human

Based on a search of the last ten years of articles related to the topic, two study articles on the potential of noni as an antidiabetic in humans were obtained. A study in Germany has been carried out to evaluate the effect of noni fruit juice on blood glucose levels and other serum parameters in Type 2 DM patients. The juice consisted of 89% puree of noni fruit mixed with 11% blueberry juice and red wine. This mixture aims to mask the unpleasant taste of Noni fruit. The results show that NFJ (Noni fruit juice) consumption for eight weeks can significantly reduce blood glucose levels in Type 2 DM patients. NFJ consumption can also significantly reduce HbA1c and hs-CRP values. A decrease in hs-CRP levels indicates an anti-inflammatory effect from the NFJ. C-peptide and HDL levels increased while total cholesterol decrea-sed. However, the increase and decrease in these three parameters' value is insignificant. The increase in C-peptide secretion indicates that the NFJ may be able to control glucose levels through insulin synthesis or insulin secretion by pancreatic β-cells. Daily NFJ consumption can potentially control increased blood glucose levels and other parameters in Type 2 DM patients[30].

A study in Indonesia used noni juice to evaluate its potential to reduce blood glucose levels in DM patients. This study was conduc-ted on 16 patients with type 2 DM. Based on statistical analysis, there was a significant difference between blood glucose levels in the control group and the intervention group. Noni fruit contains flavonoid compounds that can cause a decrease in blood glucose levels[31].

CONCLUSION

Noni (*Morinda citrifolia L.*) has an antidiabetic effect by lowering blood glucose levels and improving other parameters. Noni parts that have the potential to control Type 2 DM are fruit and leaves, which can be in the form of extracts, juices, or fermented products. Further research is needed to evaluate the toxicity, the content of active compounds, and the expression of genes related to Type 2 DM to ensure the mechanism of noni in controlling hyperglycemia. Human studies with more respondents are also needed to confirm the findings of existing studies. Based on human studies, noni fruit juice can be a suitable addition to a diet menu for Type 2 DM patients.

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